metrial cells. The Papanicolaou smear is but a screening test, and under ideal conditions there is a false-negative rate of 5% for intraepithelial disease and of 20% to 30% for invasive carcinoma of the cervix.

Once an abnormal result is obtained from a smear, the cervix should be examined colposcopically. The location and extent of the lesions can be delineated and possible extension towards and into the endocervical canal ascertained. Distinction can be made between intraepithelial and invasive cancer and histologic correlation can be obtained by biopsy and endocervical curettage. The technique of colposcopy is described in various publications.

When the entire lesion is visible and histologic and cytologic examinations show mild to moderate dysplasia, the treatment of choice is cryotherapy or, where available, laser evaporation. When there is disease in the endocervical canal, conization of the cervix is recommended. In cases where there is severe dysplasia or carcinoma in situ (cervical intraepithelial neoplasia grade III) and the whole lesion is visible, there is controversy whether cryotherapy or laser evaporation is appropriate, as the incidence of residual disease or subsequent invasive cancer seems higher than in those treated by conization.

The American Cancer Society has recently recommended changing the screening from one to three years, but the American College of Obstetricians and Gynecologists disagrees and recommends annual smears for all sexually active women because the risks of invasion in patients with undetected carcinoma in situ, or cervical intraepithelial neoplasia, increases exponentially as the interval between cytologic examinations increases. CAROLINA A. BRAGA, MBBS

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Human In Vitro Fertilization and Embryo Transfer

THE EXTRACORPOREAL fertilization of mammalian oocytes was first reported more than 20 years ago. Since that time more than ten different species of mammalian oocytes have been successfully fertilized in vitro. In the past three years, reports of successful human in vitro fertilization and embryo transfer have been received from England, Australia and the United States. The use of an in vitro fertilization and embryo transfer system to deal with various factors encountered in infertility situations is becoming more common.

Currently clomiphene citrate or human menopausal gonadotropin (Pergonal) therapy is used as the primary method to stimulate multiple follicle development and indirectly help time laparoscopic oocyte recovery. In conjunction with ovarian stimulation, patients have daily ultrasound scanning of the ovaries and serum specimens are taken for measurement of estradiol levels. Before laparoscopic aspiration, human chorionic gonadotropin is given to initiate final maturation of the oocyte.

With the use of ovarian stimulation and intravenous administration of human chorionic gonadotropin, it has been shown that laparoscopy should be done 36 hours from the time of the latter injection. The laparoscopy is done using general anesthesia and routine laparoscopic techniques. A special oocyte-aspirating system is currently being used in which a 14-gauge needle with an interlining of 18-gauge Teflon goes into a fluid trap and is connected to a wall suction set at about 150 mm of mercury negative pressure. By monitoring with combined ultrasonic and hormonal methods and with the Teflon-lined aspirating system, we are able to recover oocytes in about 85% of the follicles aspirated.

About five hours after the laparoscopic recovery of the mature oocyte, the husband is asked to produce a semen specimen. After preincubation of the sperm, 50,000 motile cells are then added to the plate containing the oocyte. At about 40 hours from the time of fertilization, the oocytes are inspected and at this time four- to eight-cell embryonic development should be observed. Once normal embryonic development is seen, transfer back into the patient's uterus is undertaken, using a Teflon catheter system.

Work on the human in vitro system began early in 1970; however, pregnancies have occurred only within the past five years. The overall pregnancy rate in any given program is about 15% to 20% of patients treated. The problems we face today with this fertility procedure are slowly being solved. The techniques that may become applicable in the near future are ultrasound-directed, needle aspiration of mature oocyte, thus alleviating the need for general anesthesia and laparoscopic aspiration. Moreover, with growing evidence of successful cryopreservation techniques in animals, the possibility of human embryo cryopreservation may become a reality. These techniques appear viable but must be tested extensively before they are available for use in humans. RICHARD P. MARRS, MD

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The Use of Ultrasound in Infertility Management

ESTIMATES ARE that one out of every six couples requires medical assistance to achieve a pregnancy. For most of these, where no pathologic condition exists, precise timing of ovulation is the most critical element for success. Whereas the use of drugs such as clomiphene citrate (Clomid) or menotropins (human menopausal gonadotropin [Pergonal]) often better define the ovulatory period, the more conventional mea-

sures rely upon basal body temperature charts, cervical mucus examination and previous menstrual history as guides. In some cases, hormone assays like rapid estradiol or luteinizing hormone have been of great use; even when all of these measures are used accurately, however, predicting the time of ovulation can be a significant clinical problem. Because the viable lifespan of a human ovum is 16 to 18 hours and preceding fertilization the sperm must undergo a four- to six-hour transformation termed capacitation, precise timing becomes critical.

This problem has been substantially eliminated in the past two years through in vitro fertilization programs and application of real-time ultrasound as a means of timing laparoscopic recovery of ova. Using a full-bladder technique, ovaries and their developing follicles can be readily defined in transverse and longitudinal planes. Follicular growth proceeds at a rate of 1 to 3 mm a day, with a rapid growth spurt possible some 24 to 36 hours before ovulation. Follicles are considered to be functionally mature when their maximal diameter is 18 mm or more. Follicles of this size will respond to ovulation doses of human chorionic gonadotropin (5,000 to 10,000 IU) within 12 to 36 hours after intramuscular injection.

Ultrasound used in this manner does not replace more conventional measures of impending ovulation, but it does hold the promise of better understanding of a given patient's ovarian response to natural or drug-induced signals. Completed studies suggest that its use increases pregnancy rates while shortening course of treatment.

PAUL S. WEATHERSBEE, PhD

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Changing Views on the Management of Vaginitis

THERE HAVE BEEN a number of significant advances in the treatment of infectious vaginitis in the past five years, not only through the introduction of new drugs but also by using existing drugs for new indications. In view of the fact that the three major types of vaginitis are all to some extent sexually transmitted, it is likely that the number of women seen with complaints referable to vaginitis will continue to increase.

The most common cause of infectious vaginitis is *Gardnerella vaginalis* vaginitis, previously called *Haemophilis vaginalis* vaginitis or nonspecific vaginitis. The infection is characterized by a profuse, homogeneous, adherent gray discharge that is associated with a "fishy" odor and a minimum of irritative symptoms. Although the laboratory diagnosis has relied on recognition of "clue cells" in the saline wet mount, another helpful diagnostic maneuver is the "odor" or "amine" test in which the odor of the discharge worsens upon adding 10% potassium hydroxide solution to the residue on the posterior blade of the speculum. Treatment has traditionally consisted of topically applied sulfa creams or oral tetracycline, but it is now generally agreed that these measures are relatively ineffective and that the agent of choice is metronidazole, 500 mg given twice a day for seven days to both the patient and her partner. In patients in whom metronidazole is contraindicated (such as pregnant women), cephalexin or ampicillin, 500 mg given four times a day for seven days, are secondary drugs of choice. A contrary opinion was recently given by Robbie and Sweet when they reported their reservations regarding the extensive and repetitive use of metronidazole because of its possible mutagenicity and carcinogenicity when more innocuous methods are available. They suggest that local preparations or ampicillin be used as the treatment of choice and that metronidazole be reserved for initial treatment failures.

Women with monilial vaginitis usually have vaginal and vulvar itching and burning and a nonodorous white vaginal discharge. Diagnosis is made on the basis of identification of pseudohyphae on a 10% KOH slide or with a positive yeast culture. Nystatin, which had previously been the drug of choice, has now been replaced by the more effective synthetic imidazole fungicides, clotrimazole and miconazole nitrate, which are available as creams, vaginal tablets and suppositories. Although standard therapy consists of a daily application for seven days, a recent study has shown equivalent results with twice-a-day therapy for three days, thereby giving patients a choice of regimens.

Trichomonas vaginalis vaginitis presents as vaginal itching and burning in conjunction with a foul-smelling watery discharge. Diagnosis depends on the identification of motile trichomonads on saline wet prep or a positive Diamonds culture. The mainstay of treatment continues to be metronidazole, though recent studies have shown that a 2-gram single dose is as effective as the more standard seven-day course. Because of improved compliance and minimization of the duration of side effects, most authors consider the single-dose regimen, given to both patient and partner, to be the treatment of choice for vaginal trichomonas.

MICHAEL S. POLICAR, MD

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Glucocorticoids and Lecithin-Sphingomyelin Ratio

THE ANTENATAL USE of glucocorticoids to prevent respiratory distress syndrome in premature infants has accelerated over the past several years. The rationale for their use is based on several studies done of humans and animals that have shown the following: (1) Exogenously administered steroids accelerate the normal pattern of lung development, including the accumula-